

MAR - 9 2004

510(k) SUMMARY

SUBMITTED BY: BECTON, DICKINSON AND COMPANY
7 LOVETON CIRCLE
SPARKS, MD 21152

CONTACT: COLLEEN A. KISTLER
TELEPHONE: (410) 316-4988

PREPARED: MARCH 5, 2004

DEVICE NAME: BD ProbeTec™ ET *Legionella pneumophila* (LP) Amplified DNA Assay

PREDICATE

DEVICES: Bacterial culture methods, Bartels Legionella Urinary Antigen ELISA Test, Binax NOW™ Legionella Urinary Antigen Tests, Medical Diagnostic Technologies' Polyvalent Fluorescent Antibody Reagents for Legionella, Gen-Probe Legionella Rapid Diagnostic System, BD ProbeTec™ ET assays for *Mycobacterium tuberculosis* Complex (ctb) Culture Identification and *Chlamydia trachomatis*/ *Neisseria gonorrhoeae* (CT/GC).

INTENDED USE: The BD ProbeTec™ ET *Legionella pneumophila* (LP) Amplified DNA Assay, for use with the BD ProbeTec™ ET System, employs Strand Displacement Amplification (SDA) technology for the direct qualitative detection of *L.pneumophila* DNA (serogroups 1-14) in sputum from patients with a clinical suspicion of pneumonia. It is intended to aid in the presumptive diagnosis of Legionnaires' disease in conjunction with culture and other methods.

DEVICE DESCRIPTION:

The BD ProbeTec™ ET LP Amplified DNA Assay is a new test designed for use on the BD ProbeTec™ ET System. The test is indicated for use with sputum specimens from patients with a clinical suspicion of pneumonia as an aid in the presumptive diagnosis of Legionnaires' disease in conjunction with culture and other methods.

The BD ProbeTec™ ET LP Amplified DNA Assay is based on the simultaneous amplification and detection of target DNA sequences using nucleic acid primers and fluorescently-labeled detector probes in a process known as strand displacement amplification (SDA). The SDA reagents are dried in two separate disposable microwells. Processed sample containing DNA is added to a Priming Microwell, which contains the amplification primers, fluorescently-labeled detector probes, and other reagents necessary for amplification. Following incubation, the reaction mixture is transferred to an

Amplification Microwell, which contains two enzymes (a DNA polymerase and a restriction endonuclease) necessary for SDA. The Amplification Microwells are sealed to prevent contamination and then incubated in a thermally controlled fluorescent reader, which monitors each reaction for the generation of amplified products. Each reaction coamplifies and detects an Internal Amplification Control (IAC), as well as the target DNA. The purpose of the IAC is to verify that proper conditions exist for amplification and to reduce the possibility of reporting a false negative result due to specimen inhibitors. The presence or absence of *L. pneumophila* DNA is determined by calculating PAT scores (Passes After Threshold) for the specimen based on predefined threshold values. The instrument automatically reports the results as positive, negative or indeterminate.

DEVICE COMPARISON:

FDA regulates assays, serological reagents, and diagnostic test systems intended to directly or indirectly, detect antigens, antibodies, or nucleic acids for identification of *Haemophilus* organisms (including *Legionella*) as class II medical devices pursuant to 21 C.F.R. § 866.3300. Within this device classification, FDA has established three *Legionella* specific product codes, including: (1) “LQH” for reagents used to detect *Legionella* nucleic acids; (2) “MJH” for enzyme linked immunosorbent assays to detect antigens from or antibodies specific to *Legionella*; and (3) “LHL” for fluorescent labeled antibody reagents with specific reactivity to *Legionella* antigens used in direct and indirect detection methods.

The BD ProbeTec™ ET LP Amplified DNA Assay is substantially equivalent¹ to other legally marketed diagnostic methods and in vitro diagnostic (IVD) medical devices for the detection of *L. pneumophila* as an aid in the diagnosis of Legionnaires’ disease. Specifically, the BD ProbeTec™ ET LP Amplified DNA Assay is a nucleic acid amplification detection assay indicated for use with sputum specimens from patients with a clinical suspicion of pneumonia as an aid in the presumptive diagnosis of Legionnaires’ disease in conjunction with culture and other methods. Thus, the BD ProbeTec™ ET LP Amplified DNA Assay has the same intended use and similar indications for use as bacterial culture methods and antigen detection tests intended to detect the presence of *L. pneumophila* in human specimens as an aid in the diagnosis of disease.

¹/ The term “substantial equivalence,” as used in this 510(k) notification, is limited to the definition of substantial equivalence as found in the Federal Food, Drug and Cosmetic Act, as amended and applied under 21 C.F.R. Part 807, Subpart E, under which a device can be marketed without premarket approval or reclassification. A determination of substantial equivalency under this notification is not intended to have any bearing whatsoever on the resolution of patent infringement suits or any other patent matters. No statements related to, or in support of, substantial equivalence herein shall be construed as an admission against interest under the US Patent Laws or their application by the courts.

Additionally, the BD ProbeTec™ ET LP Amplified DNA Assay has the same principles of operation and technological characteristics of diagnostic test systems intended to detect nucleic acids from infectious organisms, such as the Gen-Probe Legionella Rapid Diagnostic System, as well as the BD ProbeTec™ ET assays for *Mycobacterium tuberculosis* (the “ctb” assay) and *Chlamydia trachomatis*/*Neisseria gonorrhoeae*/ (or “CT/GC” assay). Specifically, the BD ProbeTec™ ET LP Amplified DNA Assay and the predicate devices are tests that employ amplification and detection of target nucleic acid regions using nucleic acid primers and fluorescently labeled detector probes. Target nucleic acids (i.e., DNA or ribosomal RNA) from specific infectious organisms in a patient's sample are amplified using specific enzymes. The amplified target molecules are detected by measuring the fluorescent signal generated by the detector probes. While the specific primers, enzymes, amplification/detection technology, fluorescent probes, and internal controls differ from test to test and organism to organism, the principles of operation for the BD ProbeTec™ ET LP Amplified DNA Assay and the predicate devices are similar.

Several minor differences exist between the BD ProbeTec™ ET LP Amplified DNA Assay and the predicate devices. For example, the BD ProbeTec™ ET LP Amplified DNA Assay detects specific nucleic acid sequences of the *L. pneumophila* organism, while reference culture detects only viable organisms. Similarly, urinary antigen tests detect soluble *L. pneumophila* serogroup 1 antigens present in human urine samples, while the BD ProbeTec™ ET LP Amplified DNA Assay detects DNA from serogroups 1 to 14 in lower respiratory specimens. Lastly, the specific primers and probes used in the BD ProbeTec™ ET LP, ctb and CT/GC Assays differ in their specificity for different nucleic acid sequences.

However, these minor differences do not raise new questions of safety and effectiveness related to the BD ProbeTec™ ET LP Amplified DNA Assay. In fact, the questions of safety and effectiveness are the same – does each test detect the presence of an infectious organism, and do the technological characteristics of each test generate a reproducible result that may be used as an aid in the diagnosis of disease. Analytical and clinical data summarized below support the position that these minor differences have no significant impact on the safety, efficacy, or performance of the assay compared to the reference and predicate methods.

SUMMARY OF PERFORMANCE DATA:

ANALYTICAL STUDIES:

The threshold values for both the *L. pneumophila* target DNA and the IAC were initially established using Receiver Operator Characteristic curve analyses of data obtained from positive and negative controls. These threshold values were verified in clinical studies and with retrospective *L. pneumophila* positive and negative lower respiratory specimens. The threshold values were then validated in additional clinical studies described below. Additional studies, including analytical sensitivity, analytical specificity, interfering substances, and reproducibility were also conducted with acceptable results.

CLINICAL STUDIES:

Prospective Study: A prospective study evaluating the performance of the BD ProbeTec™ ET LP Amplified DNA Assay was conducted using culture at seven clinical centers within the United States and Canada during the 2002 –2003 respiratory season. A total of 406 subjects were enrolled, from whom a total of 114 sputum specimens collected from 114 patients met the criteria for inclusion in the study. In comparison to culture, 100% of the prospective sputum specimens (114/114; 95% confidence interval of 96.8% - 100%) were negative by both culture and the BD ProbeTec™ ET LP Amplified DNA Assay. Because there were no culture positive specimens, there were insufficient data to estimate sensitivity. Therefore, a secondary retrospective analysis was conducted.

Retrospective Study: To aid in estimating assay sensitivity, the BD ProbeTec™ ET LP Amplified DNA Assay was evaluated with 83 retrospective sputum specimens acquired from clinical sites within the United States, Europe, and Canada. In comparison to culture, 23 of the 83 retrospective specimens were positive for *L. pneumophila*, while 60 were negative. Of these, 21 of the 23 culture positive specimens were positive in the BD ProbeTec™ ET LP Amplified DNA Assay (21/23, 91.3% agreement; 95% confidence interval of 72% - 98.9%). Two specimens were culture positive, BD ProbeTec™ ET LP Amplified DNA Assay negative. Polymerase Chain Reaction (PCR) testing was performed on both specimens; one specimen was positive by PCR. Additionally, 52 of the 60 culture negative specimens were negative in the BD ProbeTec™ ET LP Amplified DNA Assay (52/60, 86.7% agreement; 95% confidence interval of 75.4% - 94.1%). Eight specimens were culture negative, BD ProbeTec™ ET LP Amplified DNA Assay positive. PCR testing was performed on six of the eight specimens; all six specimens were positive by PCR. Overall agreement between culture and the BD ProbeTec™ ET LP Amplified DNA Assay for the retrospective specimens was 88% (73/83; 95% confidence interval of 79% to 94.1%). The 23 culture positive specimens were distributed among the following serogroups: 47.8% (11/23) Serogroup 1; 17.4% (4/23) Serogroup 3; 13.0% (3/23) Serogroup 4; 4.3% (1/23) Serogroup 5; 4.3% (1/23) Serogroup 6 and 13% (2/23) Serogroup information not available.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAR - 9 2004

Ms. Colleen Kistler
Regulatory Affairs Specialist
Diagnostic Systems
Becton Dickinson and Company
7 Loveton Circle
Sparks, MD 21152

Re: k033861
Trade/Device Name: BD ProbeTec™ ET *Legionella pneumophila* Amplified DNA
Assay
Regulation Number: 21 CFR 866.3300
Regulation Name: Haemophilus spp. serological reagents
Regulatory Class: Class II
Product Code: LQH
Dated: December 11, 2003
Received: December 12, 2003

Dear Ms. Kistler:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

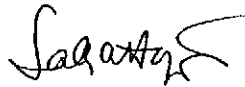
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

Page 2

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K033861

Device Name: BD ProbeTec™ ET *Legionella pneumophila* Amplified DNA Assay

Indications For Use:

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Prescription Use ✓
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)


Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K033861